

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 46313.WO01	FOR FURTHER ACTION	See item 4 below
International application No. PCT/GB2004/005090	International filing date (day/month/year) 03 December 2004 (03.12.2004)	Priority date (day/month/year) 05 December 2003 (05.12.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant CAMBRIDGE BIOTECHNOLOGY LIMITED		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).
2. This REPORT consists of a total of 7 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Date of issuance of this report 07 June 2006 (07.06.2006) Authorized officer Nora Lindner Telephone No. +41 22 338 89 65
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 18 MAY 2005

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To:

see form PCT/ISA/220

03/6-

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/005090

International filing date (day/month/year)
03.12.2004

Priority date (day/month/year)
05.12.2003

International Patent Classification (IPC) or both national classification and IPC
C07H1/00, C07H19/16

Applicant
CAMBRIDGE BIOTECHNOLOGY LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/005090

Box No. 1 Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/005090

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ not paid additional fees.
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☒ all parts.
 - ☐ the parts relating to claims Nos.

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-35, 37-39, 41-44
	No: Claims	36,40
Inventive step (IS)	Yes: Claims	1-19
	No: Claims	20-44
Industrial applicability (IA)	Yes: Claims	1-44
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item IV.

The separate inventions/groups of inventions are:

1-19

Methods of synthesising compound I of claim 1 via 2-nitro-pentabenzoyl adenosine, methods for synthesising intermediates, 2-nitro-pentabenzoyl adenosine itself and methods and uses pertaining thereto.

20-44

Methods of synthesising compound I of claim 20 via 2-nitro-pentaacetyl adenosine, the compounds of claims 36 and 40 and methods for synthesising intermediates.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

1.i). According to Rule 13.1 PCT, "The International application shall relate to one invention only OR to a group of inventions so linked as to form a single general inventive concept".

1.ii). This is further clarified in Rule 13.2 PCT, which details that "the requirement for unity of invention shall only be fulfilled when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features that defines a contribution which each of the claimed inventions, considered as a whole makes over the prior art".

2.i). For the purposes of unity, a single general inventive concept is required. This means that the problem to be solved by the claimed subject matter of the application as a whole has to be determined (i.e. to cover all claimed possibilities).

2.ii). It is considered that the problem to be solved by the present application is :
The provision of the compounds of claims 36 and 40, the intermediate of claim 14 and methods of their synthesis.

The way the applicant solves this problem is through provision of several methods which

have in common that they proceed through a pentaacylated adenosine derivative.

A priori, the only feature, of the present application, which appears capable of being the special technical feature, is the presence of a modified adenosine derivative (this may be a 2-substituted derivative according to claim 40 or a pentaacyl adenosine derivative according to claims 1-39, 41-44).

3.i). The following documents are cited:

D1 = M.J. Wanner et al. Bioorg. and Med. Chem. Lett. 10 (2000) 2141-2144

D2 = R.T. Bartlett et al. J. Med. Chem. 24 (1981) 947-954

3.ii). D1 and D2 disclose the synthesis of 2-methoxyadenosine, where the synthesis disclosed in D1 is via 2-nitro-pentaacetyl adenosine.

3.iii). Thus, D1 solves the problem in an analogous manner to the present application. In the light of the documents D1 and D2 the presence of a modified adenosine derivative cannot be regarded as the special technical feature which links together the separate inventions disclosed in the present application.

3.iv). Since there are no apparent other features which may be regarded as the special technical feature, which could link the different inventions of the application, then there is a lack of unity a posteriori.

Re Item V.

Reference is made to the following documents:

D1 = M.J. Wanner et al. Bioorg. and Med. Chem. Lett. 10 (2000) 2141-2144

D2 = R.T. Bartlett et al. J. Med. Chem. 24 (1981) 947-954

D3 = P.Y.F. Deghati et al. Tetrahedron Letters 41 (2000) 1291-1295

D4 = W. Bergmann, M.F. Stempien Jr. J. Org. Chem. 22 (1957) 1575-1577

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2004/005090

Novelty

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 36, 40 is not new in the sense of Article 33(2) PCT.

The documents D1-D4 disclose 2-methoxyadenosine, falling within claims 36 and 40. Those claims therefore lack novelty.

Inventive step

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 20-44 does not involve an inventive step in the sense of Article 33(3) PCT.

The document D1 is regarded as being the closest prior art to the subject-matter of claims 20-44, and discloses the synthesis of 2-methoxy adenosine via 2-nitro-pentaacetyl adenosine.

- The subject-matter of claims 20-44 therefore differs from this known subject matter in that the procedure is optimised in order to obtain a higher yield or a more pure compound I.
- The problem to be solved by the present invention may therefore be regarded as the provision of further methods to obtain compound I.

The solution proposed in claims 20-44 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

The skilled person would, in order to solve the above problem and having knowledge of D1, apply the various optimisation procedures described in claims 20-44. Those claims therefore lack an inventive step.